REMARKS

The Office Action of July 10, 2003 has been received and carefully considered. In response thereto, this Amendment has been submitted. It is submitted that, by this amendment, all bases of rejection and objection are traversed and overcome. Reconsideration is, therefore, respectfully requested.

Claims 29 and 30 currently stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner indicates that this is a new matter rejection.

The Examiner indicates that claim 29 recites the method step of positioning a volume of substance on a suitable testing apparatus. The Examiner indicates that the specification and originally filed claims lack clear support for the invention set forth in claim 29 and claim 30, which depends from claim 29. The Examiner has rejected the Applicant's indication of inferred support from claim 3. The Examiner indicates that the limitation of claim 3 recites "interaction" of the testing substrate, but does not support the limitation of claim 29, which recites a method step of how the "volume of the cellular material" is placed (i.e. positioned) on the "testing substrate." Therefore, the Examiner concludes the scope of the invention as originally disclosed in claim 3 would not encompass the scope of the limitation of the method step of positioning the volume of a substance containing cellular material on a suitable testing apparatus. The Examiner requires that literal support be provided for a step claiming that a material or substance is positioned. Presentation of a mere fact that a material is present on a substrate is considered insufficient to support an inference that a positioning step must have occurred to place it there.

The Examiner has invited the applicant to present a detailed analysis as to why the claimed subject matter has clear support in the specification. The Examiner's attention is directed to paragraph [0028], which states: "In the second embodiment, the operator of system 10 *dispenses* the cellular material onto the receiving surface. In the third embodiment, the cellular material *is dispensed into dimensional rectangular rray."* It is respectfully

submitted that th phras "disp nsing onto a surfac " is considered suffici ntly analogous to the term "positioning" to provide adequate support in the specification for the applicant's invention as set forth in claims 29 and 30. Thus, it is submitted that the applicant's invention as set forth in claims 29 and 30 meet the provisions of 35 U.S.C. § 112, first paragraph.

Claims 27 and 28 currently stand rejected under the provisions of 35 U.S.C. § 112, second paragraph, as failing to provide antecedent basis for the term "removable cartridge". Claims 27 and 28 have been amended by this action. It is respectfully submitted that the applicant's invention as set forth in claims 27 and 28 now particularly point out and distinctly claims the subject matter that the applicant regards as the invention.

Claims 31-35 have been amended in view of the Examiner's concerns regarding being drawn to a non-elected invention. Claims 31-35 now depend from claim 1 to contain all of the limitations found therein. It is submitted that the subject matter of claims 31-35 is properly considered with Group I.

Claims 1-10 and 27-30 currently stand rejected under 35 U.S.C. § 102(b) as being unpatentable over the Stylli reference (U.S. Patent No. 5,985,214). The Examiner indicates that the Stylli reference teaches an automated method and system for identifying chemicals having useful activity such as biological activities and collecting information resulting from such process. The Examiner indicates that the method disclosed in Stylli comprises testing a therapeutic chemical for modulating activity of a target such as cell surface proteins in a cell-based assay. The Examiner also indicates that the method disclosed in Stylii comprises the step of dispensing the reagents into the addressable sample wells, which contain a predetermined volume of the sample which, for purposes of examination, the Examiner to be equivalent to material cellular material that is at least one of whole cells and recognizable material derived from intact cells as this defined in the present application. The Examiner has not proffered support for this assumption making it difficult to fully address this point.

For purposes of examination, the Examiner considers the reagents disclosed in Stylli to be equivalent to potential pharmacologically active agents as that term is defined in the present invention. The Examiner has not proffered

evidence of this equivalency making it difficult for the applicant to fully address this point.

The Examiner indicates that the Stylli reference teaches an electrically sensitive volume displacement unit capable of dispensing a predetermined volume of 1 to 500 picoliters. The wells are considered to be arranged in a two-dimensional array such as a 96-well plate. The method is considered to include storing, managing, and retrieving data collected from the assay process. The Examiner also indicates that the automated method can comprise multiple dispensers for dispensing different reagents in a complex screening process. Based upon this analysis, the Examiner concludes that the Stylli reference anticipates the presently claimed invention as set forth in claims 1-10.

The Styll reference is directed to a mechanism that is capable of performing automated processes to accomplish various biomolecular synthetic processes. In contrast, the present invention is directed to a method which facilitates the rapid observation and ascertainment of pharmacological effect of materials on cells or recognizable cell components. Such information is of particular importance in medical fields where knowledge of drug susceptibility or resistance is valuable in determining treatment options. Two non-limiting examples of such are determination of antibiotic resistance in bacteria and determination of oncological sensitivity in cancer cells such as leukemic clonal cells. It can be appreciated that a method that facilitates determination of antibiotic resistance can contribute to the proper diagnosis and treatment of patients while avoiding administration of unnecessary or inappropriate antibiotics. A method which permits analysis of oncological efficacy in vivo can assist in the administration of chemotherapeutic drugs which are optimized for oncolgical effectiveness on the unique cancer cells of the specific patient while permitting the discontinuance of drugs for which the cancer cells have developed disease resistance. This can have great utility in customizing drug therapy treatment of cancer and other diseases.

Claim 1 currently stands rejected under 35 U.S.C. § 102(b) as being anticipated by th Stylli reference. Th applicant's invention as set forth in claim 1 is direct d to an automated method for analyzing substances. The method as set

forth in claim 1 involv s activ ting a test apparatus having at least one liquid ejection device. The liquid ejection device acts in cooperation with an electronically activated printhead to dispense a first defined volume from the liquid ejection device into contact with at least one defined volume of a substance containing cellular material. The cellular material is at least one of whole cells and recognizable cellular components from intact cells. Support for this is found in the specification at Paragraphs [0009] and [0037].

The method as set forth in Claim 1 also includes the step of detecting changes in the at least one defined volume of the substance containing cellular material triggered by introduction of the first defined volume of the potential pharmaceutically active agent. The method as set forth in claim 1 also includes the step of generating information indicative of an effect of the at least one potentially active agent on the cellular material and analyzing the generated information to generate a correlation factor.

It is respectfully submitted that the Stylli reference is directed to a device in which assay components can be analyzed and utilized for chemical reaction. The reference is concerned with utilizing molecular probes and/or die loads to ascertain reactions such as receptor activation, cellular discharge of materials such as those associated with g-protein-receptors, intercellular cyclic nucleotides, and the like. Where cell are employed, they are utilized for their capacity to posses a protein target in a sufficient quantity for measurement in a cellular assay. It is contemplated in Stylli that these expressed materials may result in pharmaceutical compositions which are prepared for storage and subsequent administration. Thus, the Stylli reference is directed, ultimately, to the production of material rather than the confirmation of affect on cellular material as would be required in evaluating a potential pharmaceutically active agent. For these reasons, it is submitted that the Applicant's invention as set forth in claim 1 is not taught, anticipated, or rendered obvious by the Stylli reference.

Claims 2-9 and 27-30 currently stand rejected under 35 U.S.C. § 102(b) as being anticipated by the Stylli reference. Claims 2-9 and 27-30 depend either directly or indirectly from claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set

forth in claims 2-9 and 27-30 is not taught, anticipated, or rend r d obvious by the sited reference for the reasons discussed previously in conjunction with claim 1.

Claim 10 also stands rejected under 35 U.S.C. § 102(b) as being anticipated by the Stylli reference. Claim 10 depends from claim 1 to specify that the method comprises a further step of interactively activating at least one second liquid ejection device to dispense a second defined volume of a potential chemically active substance into contact with the defined volume of the substance containing cellular material. It is submitted that the Stylli reference fails to teach or suggest the step of interactively activating at least one second liquid ejection device. For this reason and for the reasons discussed previously in conjunction with claim 1, it is submitted that the applicant's invention as set forth in claim 10 is not taught, anticipated, or rendered obvious by the Stylli reference.

Claims 1-10 and 27-30 currently stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Balch (US Patent 6,083,763) in view of Stylli (US Patent 5,985,214). The Balch reference is cited as disclosing a method of drug screening in which the drug to be screened reacts with biosite comprising biologically derived molecules deposited on the top surface of the substrate in a 96-well sample plate. The 96-well sample plate is scanned by a scanning mechanism to produce an image.

The Stylli reference is cited as teaching an automated method and system for identifying chemicals having useful activities such as biological activities and collecting information resulting from such a process. The Examiner cites the Stylli reference as disclosing a method comprising the step of testing a therapeutical chemical for modulating activity of a target such as cell surface proteins in a cell-based array. The disclosed method is also considered to comprise the step of dispensing reagents into addressable sample wells containing predetermined volumes of the sample. Electrically sensitive volume displacement unit can dispense predetermined volumes between 1 and 500 picoliters. The wells can be arranged in a two-dimensional array such as a 96-well plate. The method is also taken to include storing, managing and retrieving data collected from the assay process. The Examiner concludes that the Stylli reference would provide th advantage of reducing th volume of sample processes and consumable cost.

The Examiner also indicates that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the method of dispensing drug onto the cellular material as taught by Stylli in the method of Balch. The Examiner concludes that one of ordinary skill in the art would have been motivated to include the method of dispensing drugs onto the cellular material in the method of Balch for the advantage of providing a reduction in the volume of sample processes and consumable costs as disclosed in Stylli.

The invention as presently claimed is directed to an automated method for analyzing substances containing cellular material. In the automated method, a test apparatus having at least one liquid ejection device acting in cooperation with an electronically activated printhead is activated to dispense a first defined volume into contact with a defined volume of a substance containing cellular material. The defined volume that is dispensed contains at least one potential pharmaceutically active agent.

The term "substance containing cellular material" as that term is employed in the claimed invention is defined as one that contains particular cells of interest for which evaluation of a potential pharmaceutically active material is sought. The cells of interest are typically referred to as target cells. The process can be employed on biologically intact cells as well as on recognizable material from intact cells such as mitochondria, Golgi bodies, nuclei, nucleoli, and the like. Such materials suitable for testing and analysis by the method as set forth in claim 1 are those structures generally discernable by high resolution microscopy. As set forth in claim 1, cellular material is at least one of whole cells and recognizable cellular components.

In contrast, the Balch reference is directed to testing of "biosite" material. The Balch reference defines such material as biological molecules or capture probes that are deposited on the top surface of the reaction substrate or base material. The Balch reference fails to teach or suggest a test method that can be employed on samples containing intact cells and/or recognizable material from intact cells. In contrast, the Balch reference is directed to a method of molecular probe manipulation analysis. It is respectfully submitted that the Balch reference fails to teach or suggest a method in which potential pharmaceutically active agents could be evaluated by detecting changes in the defined volume of

th substance containing cellular material and generating information indicative of the observed effect and analyzing the generated information to generate a correlation factor.

The Stylli reference lacks teaching to suggest ability and applicability in ascertaining pharmaceutical activity for the reasons previously discussed. It is submitted that the method defined in claim 1 provides accuracy, reproducibility, and, when necessary, variability in evaluation pharmaceutical activity of materials against various cells and cell colonies such as infectious bacteria and the like not taught or suggested in the Stylli reference or the Balch reference, taken alone or in combination. Furthermore, it is submitted that the references fail to teach or suggest a step in which information indicative of the effect of at least potential pharmacologically active agent on cellular material is generated and the analysis of such generated information to develop a correlation factor occurs. It can be appreciated that a method which can be efficiently utilized to ascertain drug resistance of susceptibility of infectious cells would be of great benefit in various medical applications, including but not limited to, diagnosis, pharmaceutical prescriptions, and the like. For these reasons, it is submitted that the applicant's invention as set forth in claim 1 is not taught, anticipated, or rendered obvious by the cited references.

Claims 2-6, 8, 9, and 27-30 also stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by Balch in view of Stylli. The applicant's invention as set forth in claims 2-6, 8, and 9 depends either directly or indirectly from claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set forth in claims 2-5, 8, 9, and 27-30, is not taught, anticipated, or rendered obvious by the cited references for the reasons discussed previously in conjunction with claim 1.

Claim 7 also stands rejected under 35 U.S.C. § 103(a) as being rendered obvious by Balch in view of Stylli. The applicant's invention as set forth in claim 7 is directed to an automated method in which the defined volume of the substance containing cellular material is present as a plurality of individual samples arranged in an array capable of yielding statistically viable data. It is submitted that the Balch reference fails to reach or suggest a method whereby a volume of a substance containing cellular material as defined in the present

invention is pr sent as a plurality of individual samples arranged in an array. It is submitted that the Stylli reference fails to teach or suggest dispensing a material from an ejection device having an electronically activated printhead into the volume present as a plurality of individual samples arranged as an array. Furthermore, It is respectfully submitted that claim 7 depends from independent claim 1 to contain all of the limitations found therein. By this dependency, it is submitted that the applicant's invention as set forth in claim 7 is not taught, anticipated, or rendered obvious by the cited references.

Claim 10 also stands rejected under 35 U.S.C. § 103(a) as being rendered obvious by Balch in view of Stylli. The applicant's invention as set forth in claim 10 is directed to a method which includes the step of interactively activating at least one second liquid ejection device to dispense a second defied volume of a potential pharmaceutically active agent into contact with the defined volume of the substance containing cellular material. It is respectfully submitted that the Balch and Stylli references fail to teach or suggest the dispensing of at least one second liquid into contact with the substance containing cellular material. It is respectfully submitted that the interactive and sequential dispensing of multiple materials, in combination with the generation of information and analysis permits analytical flexibility and greater complexity in analytical design. Without being bound to any theory, it is believed that administration of materials from at least one liquid ejection device having an electronically actuated printhead permits effective introduction of material into samples containing intact cells or cellular organelles in a manner which permits observation of responses and the interactive activation of at least one second liquid ejection device. Thus, it is submitted that the Stylli and Balch references fail to teach or suggest such features. Thus, it is submitted that the applicant's invention as set forth in claim 10 is not taught, anticipated, or rendered obvious b the cited references.

In summary, claims 1, 27, 28, 31, 34 and 35 have been amended. Additionally, discussion has been presented as to why the applicant's invention as set forth in claims 1-10 and 27-35 is not taught, anticipated, or rendered obvious by the cited references. In view of this amendment and the foregoing discussion, it is submitted that the applicant' invention as set forth in claims 1-10 and 27-35 is in a condition suitable for allowanc , a notice of which is r spectfully requested.

In the alternative, ntry of this Am ndment is sought for purpos s of appeal. It is respectfully submitted that this Amendment seeks to resolve and remove issues for consideration on appeal. Additionally, this Amendment provides for cancellation of claims to reduce the number of claims to be considered on appeal. Entry of this Amendment is, therefore, earnestly sought.

Respectfully submitted,

Denise M. Glassmeyer
Attorney for Applicant
Registration No. 31,831
(248) 649-9900

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3331 West Big Beaver Road
Suite 109
Troy, Michigan 48084-2813
DMG/ljo